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Mumbai - 400 013

GB/04/2731

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THE PATENTS ACT, 1970

IT IS HEREBY CERTIFIED THAT, the annex is a true copy of Application and Provisional Specification filed on 24/06/2003 in respect of Patent Application No.658/MUM/2003 of M/S. CIPLA LIMITED, 289 BELLASIS ROAD, MUMBAI CENTRAL, MUMBAI - 400 008, INDIA.

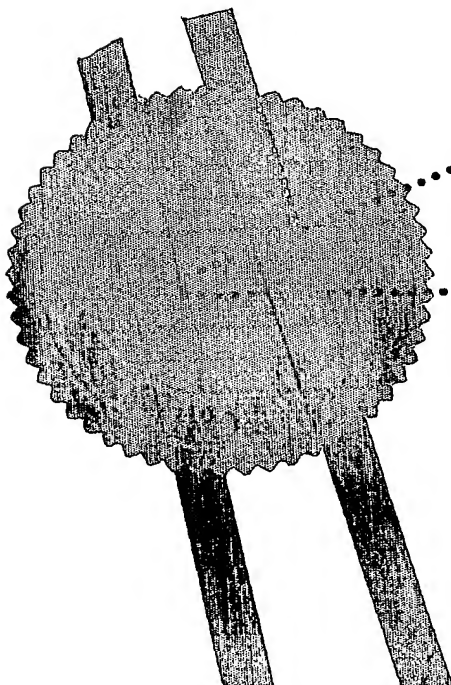
This certificate is issued under the powers vested in me under Section 147 (1) of the Patents Act, 1970.

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Dated this 17th day of August 2004.


(R. BHATTACHARYA)

ASST. CONTROLLER OF PATENTS & DESIGNS.



FORM-1
THE PATENTS ACT, 1970
(39 OF 1970)

APPLICATION FOR GRANT OF PATENT
[See Section 5(2), 7, 54 and 135 and Rule 33A]

1. We,
 - (a) **M/s. CIPLA LIMITED**
 - (b) **289 BELLASIS ROAD, MUMBAI CENTRAL, MUMBAI - 400 008, INDIA**
 - (c) **NATIONALITY - INDIAN**

2. Hereby declare-
 - (a) That we are in possession of an invention titled **"PHARMACEUTICAL DISPENSING AID"**;
 - (b) That the **PROVISIONAL SPECIFICATION** relating to this invention is filed with this application;
 - (c) That there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are:
 - (a) **Mr. LULLA, Amar**
 - (b) **131, Maker Tower-L, 13th Floor, Cuffe Parade, Colaba, Mumbai - 400 015, Maharashtra, India**
 - (c) **Indian Citizen**

 - (a) **Mrs. MALHOTRA, Geena**
 - (b) **4, Anderson House, Opposite Mazgaon Post Office, Mazgaon, Mumbai - 400 010, Maharashtra, India**
 - (c) **Indian Citizen**

658/mum/2003

24/6/2003

Received by	3060
Subscribed by	24/6/03
Vide Entry No.	3693
Register of Inventors, Mumbai.	
Date	24/6/03

4. We, claim the priority from the application filed in convention countries, particulars of which are as follows:

Not Applicable

and declare that above application or each of the above applications was the first application(s) in a convention country/countries in respect of our invention.

5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which we are the applicant:

Not Applicable

6. We state that the application is divided out of our application the particulars of which are given below and pray that this application deemed to have been filed on _____ under Section 16 of the Act.

Not Applicable

7. That we are the assignee of the true and first inventors.
8. That our address for service is as follows: -

**LEX ORBIS, INTELLECTUAL PROPERTY ATTORNEYS, B-1/39, [LGF],
MALVIYA NAGAR, NEW DELHI - 110 017**

9. Following declaration was given by the inventors or applicants in convention country:

We are the true and first inventors for this invention declare that the applicant herein is our assignee or the legal representative

Mr. LULLA, Amar

**131, Maker Tower-L, 13th Floor, Cuffe Parade, Colaba, Mumbai - 400 015,
Maharashtra, India
Indian Citizen**

Mrs. MALHOTRA, Geena

**4, Anderson House, Opposite Mazgaon Post Office, Mazgaon, Mumbai - 400 010,
Maharashtra, India**

Indian Citizen

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to me on this application.
11. Following are the attachment with the application:
- (a) Form 2 with the **PROVISIONAL SPECIFICATION** in triplicate alongwith the abstract;
 - (b) Form 3 [Statement and Undertaking under Section 8];
 - (c) Form 5 [Declaration as to Inventorship];
 - (d) Payable at Par Cheque numbered 426750 to the tune of Rs. 3,000 drawn on the Standard Chartered Bank, [Payable at Par] as Official Filing Fee.

We request that a patent may be granted to us for the said invention.

Dated this the 23rd Day of June 2003



MANISHA SINGH
Agent for the Applicant
LEX ORBIS
Intellectual Property Attorneys
B1/39[LGF], Malviya Nagar
New Delhi – 110 017

To
The Controller of Patents
The Patent Office
At Mumbai

FORM 2

The Patents Act, 1970

[39 of 1970]

PROVISIONAL SPECIFICATION

[See section 10]

1. "PHARMACEUTICAL DISPENSING AID"

2. (a) M/s. CIPLA LIMITED

**(b) 289 BELLASIS ROAD, MUMBAI CENTRAL,
MUMBAI - 400 008, INDIA**

(c) NATIONALITY - INDIAN

The following specification describes the nature of this invention: -

*Duplicate
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24.16 / 2003*

3. **PHARMACEUTICAL DISPENSING AID**

(0001) **Field of the Invention**

(0002) This invention in general relates to pharmaceutical dispensing aids. More particularly, this invention relates to an inhaler device comprising of an improved canister crimped with a valve, wherein the canister is made of polycarbonate polymer and is transparent in nature.

(0003) **Background of the Invention**

(0004) Metered Dose Inhalers are well known in the art. A metered dose inhaler typically comprises of a canister crimped with a metering valve, wherein the canister is filled with an aerosol formulation that includes a drug dissolved or dispersed in a propellant. Typically the container of the inhaler is made of jacketed glass or metal. Metallic containers are either made of tin-plated steel or aluminum. The propellants used in metered dose inhalers include chlorofluorocarbons (CFCs), hydrofluoro-carbons (HFCs) or hydrofluoroalkanes (HFAs).

(0005) Chlorofluorocarbon (CFCs) propellants are considered to cause ozone depletion. Consequent to the Montreal protocol and the call for banning of the CFC propellants, new ozone friendly propellants have been developed. These propellants include the hydrofluoroalkane (HFAs). HFAs do not contain chlorine and are considered as ozone friendly.

(0006) **Related Arts**

(0007) United States Patent Number 6444028, describes a plain aluminium can for an ipratropium formulation.

(0008) United States Patent Application Numbered 20030066525 to Lewis David et al titled 'Pressurized metered dose inhalers (MDI)' discloses a pressurized metered dose inhaler wherein the internal surface of

the inhaler consists of stainless steel or anodized aluminum or the internal surface lined with an inert organic coating.

(0009) United States Patent Application Numbered 2002219743 discloses a plastic pressure bottle having a PET layer for alkaline ingredients & manufacture of laminated bottles with outer layer & polyamide inner layer.

(0010) Japanese Patent Application No. JP 200020794 discloses a container comprising mainly PET based layer & a gas barrier layer installed in the center to the inner side of the wall. Thus a five-layered laminate for preparation of container was made from PET as two surfaces & central layer & ethylene -vinyl alc. Copolymer (F101BZ) as inner layer b/w the central layer & the surface.

(0011) The known arts, disclose canisters for metered dose inhalers, which are opaque. They therefore, do not provide the advantage of visible dosage monitoring of the content inside the container. This is especially needed when the canister contains a medicated formulation. The medicament may be in the form of solution or suspension. For suspensions, there exists the possibility of agglomeration. Agglomeration occurs mainly when the medicament is used infrequently or only when the patient's condition demands. In such cases, the same medicament is used for months either till it gets over or expires.

(0012) It is possible that due to the non-transparent nature of the container, the patient is unable to estimate the amount of dose remaining in the container. Therefore at the time of an emergency, the medicine may not be available or may be difficult to obtain.

(0013) It is also necessary that there be some indication by way of marking or otherwise to the patient about the amount of dosage form remaining in the canister. This can always indicate to the patient that now is the time to buy another canister and keep it in stock.

(0014) The above mentioned technical disadvantages associated with the known configurations of the prior art metered dose aerosol devices prompted configuring a device that enables the patient to visually monitor the form and content of the inhalation medicament contained in the aerosol device. The present invention therefore offers an improved canister made up of polycarbonate, which imparts transparency to the canister.

(0015) It has also been observed that the drug particles of the formulation do not adhere to the inner walls of the polycarbonate container thereby imparting anti-adherent property upon the canister. This also results in giving a better uniformity of dose and content per spray.

(0016) Summary of the Invention

(0017) In accordance with one embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid having a transparent canister made of materials such as polycarbonate polymers.

(0018) In accordance with another embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid having a transparent canister thus enabling the user thereof to visually monitor the content and form of the medicament contained therein.

(0019) In accordance with another embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid having a transparent canister with etchings or markings that indicate to the patient the level of the medicament inside the container.

(0020) In accordance with yet another embodiment, the present invention provides for an improved pharmaceutical dispensing aid having a canister configured to contain a medicament wherein the canister is configured to prevent adhesion of the medicament to the inner wall of the canister.

(0021) In accordance with still another embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid for administering the medicament, the improved pharmaceutical dispensing aid having a canister made of polycarbonate polymer wherein the use of polycarbonate polymer prevents adhesion of the medicament to the inner surface of the canister thus enabling uniform dose content per spray.

(0022) In accordance with another embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid for administering the medicament, the improved pharmaceutical dispensing aid having a canister made up of polycarbonate polymer wherein the use of polycarbonate polymer imparts aesthetic elegance to the container thereby making it useful in various other fields such as cosmetology, nasal sprays, dry powder inhalers, and such other related fields.

(0023) In accordance with still another embodiment, the present invention provides for configuring an improved pharmaceutical dispensing aid in the form of a metered dose inhaler device.

(0024) Detail Description of the Preferred Embodiments

(0025) The present invention describes an improved canister for spraying and inhalation. The canister is made of polycarbonate which makes it transparent.

(0026) The transparent container enables the patient to visibly monitor the content of the medicament inside the container. Therefore the patient realizes when the medicament is about to get over and keeps another canister in stock thereby avoiding situations when the patient is in urgent need of the medication and the medicament is unavailable and difficult to obtain. Transparency of the canister also enables the patient to visualize the physical nature of the medicament. This visualization is

critical when the medicament is a suspension or the medicament has not been used since a long time. For example, before inhalation, the patient shakes the canister and realizes that the drug particles do not disperse completely. In this way, the patient understands that the medicament is unstable and is not fit for inhalation. Therefore transparency of the container becomes the only means that a patient who is untrained in this field of expertise, and the ultimate user of the medicament realizes that this medicament is not to be inhaled.

(0027) The canister may also bear some markings or etchings indicative of the various levels of the content of the canister. Therefore in case of medicated formulations, especially aerosols, the patient can then inhale the doses only in the levels that produces pharmacologically therapeutic effects. Currently the patient has to guess how many doses are left in the canister and have two practical options: (1) throw away the canister that may still contain acceptable metered doses or (2) use a product when it may be beyond the recommended number of doses and risk not receiving correct drug dose. The former is wasteful, and the latter is potentially dangerous.

(0028) For example: If the metered dose inhaler is configured to deliver 120 puffs, the actual number of puffs filled inside the container is 20 to 30 more than the puffs mentioned on the label. This is because the initial few and the last few puffs do not actually contain the active ingredient in therapeutic amounts. Expulsion of the initial few doses is known as priming of the inhaler. This is necessary so that the next dose the patient inhales has the desired amount of drug in it. The last few puffs actually contain only the propellant which is necessary to expel the active. The etchings or markings are therefore indicative of the levels of the doses that are to be expelled for priming.

(0029) Usually the patient is instructed to discard the canister after inhalation of certain number of doses. This reliance on the patient's memory may cause serious casualties because the patient may forget to

discard the used canister that contains only the non-active excipients and buy a new one. Thus the markings also indicate to the patient the level after which the patient should not use the medicament as it only contains the propellant and no drug.

(0030) It has also been observed that the polycarbonate canister prevents adhesion of the active drug particles to the inner walls of the canister. This results in better uniformity of dosage and content per spray with every puff. Therefore the therapeutic performance of the canister is enhanced.

(0031) The canister has a cylindrical body having a closed end and a round base and another end having a mouth. The cylindrical body is made up of polycarbonate polymer. The mouth is crimped with a metering valve of a suitable material such as aluminium or tin. The capacity of the container may range from 2 ml to 50 ml. The said canister is filled with formulations such as medicated solutions or suspensions for inhalation.

(0032) The formulations comprise of one or more active pharmaceutical ingredients are selected from a group comprising bronchodilators, beta-2-adrenoacceptors anticholinergics, steroids, beta-2-agonists, antiallergics and such other compounds, their salts, derivative, enantiomers, prodrugs and racemic mixtures thereof. The active ingredient is combined with a propellant or a mixture of propellants selected from the class of HFA propellants. The HFA propellants may be selected from 1,1,1,2-tetrafluoroethane or 1,1,1,2,3,3,3-heptafluoropropane. The formulation may optionally comprise of other pharmaceutically acceptable excipients such as co-solvents, surfactants and the like. Ethanol may be used as a co-solvent in the range of 1-20% with respect to the formulation. The surfactants may be selected from lecithin, oleic acid, sorbitan trioleate, glycerol and the like, in the range of 0.0001-15% with respect to the active.

(0033) The transparent polycarbonate canister so designed is aesthetic and elegant and can be used in various other fields such as

cosmetology. For cosmoceutical preparations, the canister may be fitted with a continuous valve. The capacity of the canister may range from 10 ml to 500 ml or more as required. The canister may comprise of various cosmetological formulations such as deodorants, hair sprays, hair mousses, air fresheners, shaving creams etc.

(0034) The canister may be prepared by any method known in the art. One such suitable illustration of a method of preparation of the said canister is as follows:

(0035) Manufacturing process of the polycarbonate container by injection molding / injection blow molding:

(0036) The polycarbonate needed for manufacturing the can is stored in a silo as pellets. Before use, it is dried at 120° C. The injection-molding machine has a variety of the sections. There is a polycarbonate reservoir. Below is an endless screw powered by an engine, which conveys the polycarbonate to the mold. Resistance heaters melt the plastic by raising it to a temperature of 320° C. The mold has two sections, one fixed & one movable so that the part can be ejected. The mold is cooled by pressurized circulating water with a temperature of 120° C. Polycarbonate granules are loaded into hopper drier kept at 80°C-90°C so as to remove the moisture. Then these granules are injection molded/injection blow molded (Plasticized) at 220-230°C at different zones in the machine.

(0037) Abbreviations used in the text

PET	-	Polyethylene terphthalate
MDI	-	Metered Dose Inhaler
HFAs	-	Hydrofluoro Alkane
CFC	-	Chlorofluorocarbon

(0038) The following examples are for the purpose of illustration of the invention only and are not intended in any way to limit the scope of the invention.

1. Salbutamol Sulphate HFA Inhalation (200 doses).

Sr. No.	Ingredients	Quantity
1.	Salbutamol Sulphate	28.8 mg
2.	1,1,1,2-tetrafluoroethane	q.s.

2. Budesonide HFA Inhalation (200 doses).

Sr. No.	Ingredients	Quantity
1.	Ipratropium	24 mg
2.	1,1,1,2-tetrafluoroethane	q.s.

3. Budesonide HFA Inhalation (200 doses).

Sr. No.	Ingredients	Quantity
1.	Budesonide	48 mg
2.	Ethanol	2.73 gms
3.	Lecithin	0.24 mg
4.	1,1,1,2,3,3,3-heptafluoropropane	q.s.

(0039) It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and

optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be falling within the scope of the invention.

5.

ABSTRACT

An improved pharmaceutical dispensing aid such as a metered dose inhaler device comprising a transparent canister made of polycarbonate polymer is disclosed. The canister is configured to contain one or more active pharmaceutical ingredients, one propellant or a mixture of propellants along with any other pharmaceutically acceptable suitable excipients thereof in a suitable dosage form. The improved canister is transparent in nature thereby providing visual dosage monitoring to the patient.